



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

Via Federal Express

NOV 17 1999

WARNING LETTER

Lawrence D. Dorr, M.D.
[REDACTED]
[REDACTED]
[REDACTED]

Dear Dr. Dorr:

During the period of March 15 through March 26, 1999, Ms. Omotunde O. Osunsanmi, an investigator with the Food and Drug Administration's Los Angeles District Office, visited you. The purpose of the visit was to conduct an inspection to determine whether your activities and procedures as a clinical investigator participating in the investigational study of the [REDACTED] sponsored by [REDACTED] complied with applicable Food and Drug Administration (FDA) regulations. This product is a device as that term is defined under Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The inspection was conducted under a program designed to ensure that data and information contained in requests for Investigational Device Exemptions (IDE), Premarket Approval Applications (PMA), and Premarket Notifications [510(k)], are scientifically valid and accurate. Another objective of the program is to ensure that human subjects are protected from undue hazard or risk during the course of scientific investigations.

Our review of the inspection report submitted by the Los Angeles District Office revealed significant violations of Title 21, Code of Federal Regulations (21 CFR), Part 812 - Investigational Device Exemptions, and 21 CFR Part 50 - Protection of Human Subjects. These deviations were listed on the Form FDA 483, "Inspectional Observations," which was presented to and discussed with you at the conclusion of the inspection conducted at the [REDACTED]. The Form FDA 483 was annotated to reflect your promise to take corrective action(s). Deviations noted on this form are summarized below:

Failure to comply with import requirements (21 CFR 812.18).

Your records indicate that you imported into the United States (U.S.) significant risk [REDACTED] devices referred to as [REDACTED] with the intent of implanting them into patients outside of an authorized Investigational Device Exemption (IDE) study in which you were a clinical investigator.

This activity is a violation of U.S. importation requirements. Medical devices imported into the U.S. are subject to examination by the FDA at the time they are imported and are required to meet the same standards as domestic devices. The device must be safe and effective and contain informative and truthful labeling in English. At the time the device is offered for importation, it is the responsibility of the importer to assure the entry complies with all U.S. Customs Service and FDA requirements, including, but not limited to, notification, bond, product identification, and legal status. Failure of the importation to meet the entry requirements of Customs and the FDA may result in the seizure of the imported article, bond penalty assessment, or refusal of admission of the article.

Failure to obtain FDA and institutional review board (IRB) approval and informed consent before allowing subjects to participate in an investigational study (21 CFR 812.100 and 110; and 21 CFR Part 50).

- You implanted investigational devices in more than forty (40) patients without obtaining FDA and IRB approval and informed consent for participation in a research study. You implanted the unapproved devices on [REDACTED]. Some of your patients were implanted with the unapproved devices while an authorized study of the same device was ongoing. For example, on [REDACTED] approved and unapproved devices were implanted in patients [REDACTED] and [REDACTED] (non-study patient), respectively.
- You failed to provide study subjects with an adequate informed consent form containing all of the basic elements of 21 CFR 50.25, and to obtain their signature before allowing them to participate in the study. For example, review of the informed consent form used for implantation of the unapproved devices disclosed an untitled three-sentence paragraph regarding the [REDACTED] device as an investigational device. Further, the informed consent form did not contain a description of any reasonably foreseeable risks to the subjects. About twenty-nine (29) patients signed the informed consent form *after* the devices were implanted; and two (2) of these patients indicated that they were unaware of the investigational nature of the device.

Failure to conduct an investigation in accordance with the investigational plan and the conditions of approval imposed by the FDA and IRB [21 CFR 812.100 and 21 CFR 812.110(b)].

You failed to limit implantation of the investigational device to subjects randomized in accordance with the investigational plan and the IRB's approval for the investigational study. For example, you implanted the investigational device outside of the approved IDE study (G940106). In addition, you failed to adhere to the randomization scheme for the approved controlled clinical study. The randomization of test or control devices for the approved study used a system of randomly generated pairings of the devices to patient numbers. You stated in your letter to [REDACTED] dated [REDACTED] that patients "were specifically selected for metal-on-metal" outside the IDE study. You further stated, "The patients were selected because of young age, expected long life, and activity levels." The inspection report reveals that some of the patients were implanted with the unapproved device while the IDE study was ongoing. For instance, on [REDACTED] a device was implanted in IDE study patient [REDACTED] while on the same day an unapproved device was implanted in non-study patient [REDACTED]. This pre-sorting of eligible patients compromised the randomization process for the IDE study.

Failure to maintain accurate, complete, and current records relating to your participation in an investigational study [21 CFR 812.140(a) and (a)(3)(ii)].

- You failed to maintain records on the shipment, receipt, use, and disposition of devices. For example, you were in possession of fifty-seven (57) devices from Australia that you obtained outside of the authorized U.S. supply of devices. To date, you are unable to provide complete documentation of the receipt, use, and disposition of these devices. The inspection revealed that unused devices were boxed up and returned to the sponsor's sales representative for shipment to Australia. Complete records on the number of devices returned and their lot numbers are not available.
- You failed to maintain records on an adverse device effect involving [REDACTED] that occurred during the implantation of the investigational device.

As a clinical investigator, you should maintain accurate, complete, and current records relating to your participation in an investigational study, including records of adverse device effects, whether anticipated or unanticipated.

Failure to report an adverse device effect to the sponsor and IRB [21 CFR 812.150(a)(1)].

You failed to report an adverse device effect that occurred during the implantation of an investigational device. For example, while implanting the device into patient [REDACTED] a [REDACTED] occurred. This event was not reported to the sponsor or the IRB.

The deviations listed above are not intended to be an all-inclusive list of deficiencies at your site. As a clinical investigator, it is your responsibility to ensure that investigations that you participate in are conducted in accordance with applicable FDA regulations. To assist you, we have enclosed a copy of the *FDA's Import Program/General Procedures* document, and the *FDA Information Sheets*, guidance for clinical investigators.

Please advise this office, in writing, **within fifteen (15) working days of receipt of this letter** of the specific steps you have taken to correct these violations and other violations known to you, and to prevent the recurrence of similar violations in current or future studies. Failure to respond can result in further regulatory action, including disqualification, without additional notice.

You should direct your response to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, Program Enforcement Branch II (HFZ-312), 2098 Gaither Road, Rockville, Maryland 20850, Attention: Kathleen E. Swisher, R.N., J.D., Consumer Safety Officer.

A copy of this letter has been sent to our Los Angeles District Office, 19900 MacArthur, Suite 300, Irvine, California 92715. We request that a copy of your response be sent to that office as well.

Sincerely yours,



Lillian J. Gill
Director
Office of Compliance
Center for Devices and
Radiological Health

Enclosures